## REMARKS/ARGUMENTS

Claims 151-154, 158-159, 163, 165-170, 172-178, 180, 182-202 and 204-236 are currently pending and stand rejected. By way of this response, eighteen (18) claims have been amended, zero (0) independent claims have been added, zero (0) dependent claims have been added and zero (0) claims have been canceled. Applicant respectfully submits that no new matter has been added by way of this amendment. No fees are believed due.

Support for the amendment to Claim 151 can be found at least at page 31, lines 10-20 and at page 40, line15 to page 46, line 15 of the specification as originally filed.

Support for the amendment to Claim 156, 157 and 159 can be found at least at page 31, lines 10-20 of the specification as originally filed.

Support for the amendments to Claims 165 and 202 can be found at least at page 13, lines 23-25, page 24, lines 15-20, page 57, lines 20-25 and Examples I-IV, VI, VIII, X, XII-XVII. One of the amendments to Claim 165 corrects a misspelling.

Support for the amendment to Claim 191 can be found at least at page 25, lines 14-24 and page 31, lines 15-20; and at page 40 of the specification as originally filed.

Support for the amendments to Claims 152, 153, 184, 187, 188, 193, 195, 198, 199, 223 and 230 can be found at least at page 40, line15 to page 46, line 15 of the specification as originally filed.

## I. THE REJECTION UNDER 35 U.S.C. § 112, SECOND PARAGRAPH, SHOULD BE WITHDRAWN.

The Office Action rejected claims 151-154, 156-159, 163, 165-170, 172-178, 180 and 182-236 under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Without admitting or conceding in any manner that rejected claims 151-154, 156-159, 163, 165-170, 172-178, 180 and 182-236 fail to comply with 35 U.S.C. § 112, second paragraph and solely to expedite the prosecution of the present application, claims 151-153, 159, 165, 184, 187, 188, 191, 193, 195, 198, 199, 223 and 230 have been amended to remove the terms "therapeutically effective," as it relates to the amount of sodium bicarbonate, and "dosage unit." Applicant respectfully submits that this rejection is now moot, and that no new matter has been presented by way of these amendments. Withdrawal of the rejections of claims 151-154, 156-

159, 163, 165-170, 172-178, 180 and 182-236 under 35 U.S.C. § 112, second paragraph is respectfully requested.

## II. THE REJECTION UNDER 35 U.S.C. § 112, FIRST PARAGRAPH, SHOULD BE WITHDRAWN.

The Office Action rejected claims 151-154, 156-159, 163, 165-170, 172-178, 180 and 182-236 under 35 U.S.C. § 112, first paragraph, as failing to comply with the enablement requirement. Applicant respectfully requests that this rejection be withdrawn in light of the below arguments and the current amendments, made without admitting or conceding in any manner that the rejected claims fail to comply with 35 U.S.C. § 112, first paragraph and solely to expedite the prosecution of the present application. Applicant sets forth below its response to each of the factors ("the *Wands* factors") enumerated in the Office Action. *In re Wands*, 858 F.2d 731, 737, 8 U.S.P.Q. 2d 1400,1404 (Fed. Cir. 1988).

### A. The nature of the invention

According to the Office Action, "[t]he claims are drawn to composition which upon administering to a subject, will achieve a plasma concentration of omeprazole at 0.1 μg/ml; at about 30 minutes. Such a scope is highly unpredictable." The nature of the invention is the subject matter to which the claimed invention pertains. M.P.E.P. § 2164.05(a). If little is known in the prior art about the nature of the invention and the art is unpredictable, the specification would need more detail as to how to make and use the invention in order to be enabling. *See, e.g., Chiron Corp. v. Genentech Inc.*, 363 F.3d 1247, 1254, 70 U.S.P.Q. 2d 1321, 1326 (Fed. Cir. 2004). If one skilled in the art can readily anticipate the effect of a change within the subject matter to which the claimed invention pertains, then there is predictability in the art. M.P.E.P. § 2164.03.

An aspect of Applicant's discovery is that one can administer the claimed composition to attain the claim blood levels. The present specification clearly provides the detail necessary to make and use the invention. Therefore, Applicant respectfully traverses this rejection.

### B. The state of prior art and predictability or lack thereof in the art

The Office Action asserts suggests that "'plasma' concentration provided *no predictable correlation*" in the absence of "defined 'subject'; ... defined preparation of omeprazole;... frequency/order of dosing; ... carrier; [and] ... site of release after oral administration ..."

In response to the Office Action's contention that, "[t]here is no description or uniformity as to the plasma concentration and dosage relationship in species variation," Applicant submits that one skilled in the art would be able to determine plasma concentration and dosage relationship in different species, based on, for example, the embodiments of the disclosure, the pharmacological properties and activity of omeprazole and the individual subject being treated. By way of illustration and not limitation, Applicant submits that one of ordinary skill would be able to practice the claimed invention for a subject given the level of knowledge in the art and based upon page 20 lines 13-15, page 29 line 7 to page 30 line 10, page 30 line 17 to page 31 line 7, page 142 lines 14-17, the "Veterinary Formulations" set forth on pages 138-144 and the Claims in the specification as originally filed. *See In re Bundy*, 642 F.2d 430, 434, 209 U.S.P.Q. 48, 51-52 (C.C.P.A. 1981).

Furthermore, Examples I-IV at pages 48-57, Example VI at page 71, Example XI at pages 86-89, Example XVI at pages 102-110 and pages 111-162 of the specification, clearly describe and enable the claimed invention. In response to the Office Action's contention that "[t]here is no description in the specification that enteric coated or uncoated omeprazole will operate in similar manner in the instant composition," Applicant submits that one of ordinary skill in the art would be able to practice the invention based upon the prior art and the several examples on pages 48-162 of the specification as originally filed. One skilled in the art would be able to modify the teachings of the ranges in the disclosure to make and use the claimed invention. Amended claims 151 and 191 and claims depending therefrom require about 1 mg to about 100 mg omeprazole, at least a portion of which is not enteric coated, thereby providing sufficient guidance to one of skill in the art as to the preparation of omeprazole. In addition, amended claim 191 requires about 5 mEq to about 70 mEq of sodium bicarbonate. The term "milliequivalents" or "mEq" inherently relates to the acid neutralizing capacity of a buffering agent and, therefore, the skilled artisan would certainly understand how to practice this element of the invention without undue experimentation. The pharmacokinetic limitation in both claims 151 and 191 ("average plasma concentration of the omeprazole of at least about 0.1 μg/ml at any time within about 30 minutes after administration") is a functional limitation, which is understood in the art and is permissible under applicable precedent. For example, in *Geneva Pharmaceuticals, Inc. v. GlaxoSmithKline PLC*, 68 U.S.P.Q.2d 1865, 1873 (Fed. Cir. 2003), the Federal Circuit stated, "a functional limitation covers all embodiments performing the recited

function." Here, the functional pharmacokinetic language limits the claim to those buffering agents (or mixtures thereof) that provide the claimed result. *See also In re Swinehart*, 169 U.S.P.Q. 226 (C.C.P.A. 1971). Similarly, based upon the amendments and the functional limitation, one skilled in the art would be able to practice the invention and determine an appropriate carrier and site of release after oral administration. Applicant also respectfully submits that the disclosure provides for a range of omeprazole; one of skill in the art would be able to select doses falling within the claimed range that would enable one to practice the invention.

In light of the present amendments, made without admitting or conceding in any manner that the rejected claims fail to comply with 35 U.S.C. § 112, second paragraph and solely to expedite the prosecution of the present application, and above arguments, Applicant submits that this rejection is moot. Applicant submits that the presently amended claims provide enough information for one of skill in the art to determine the preparation of omeprazole, frequency/order of dosing, carrier and site of release after oral administration. In short, one of ordinary skill in the art would be able to practice the claimed invention, given the level of knowledge in the art. *See In re Bundy*, 642 F.2d 430, 434, 209 U.S.P.Q. 48, 51-52 (C.C.P.A. 1981). Therefore, Applicant respectfully requests withdrawal of this rejection.

**C. <u>The amount of guidance and working examples</u>**

The Office Action provides that "[t]here is no description or enabling information on the "plasma concentration" as to a single solid unit that will achieve the required plasma $C_{max}$." Applicant respectfully submits that the specification need not contain an example if the invention is otherwise disclosed in such manner that one skilled in the art will be able to practice it without an undue amount of experimentation. *In re Borkowski*, 422 F.2d 904, 908, 164 U.S.P.Q. 642, 645 (C.C.P.A. 1970); M.P.E.P. § 2164.02. Compliance with the enablement requirement does not turn on whether an example, working or prophetic is disclosed. M.P.E.P. § 2164.02. Since only an enabling disclosure is required, applicant need not describe all actual embodiments. M.P.E.P. § 2164.02. In addition, the Federal Circuit has held that even "a considerable amount of experimentation is permissible, if it is merely routine, or if the specification in question provides a reasonable amount of guidance with respect to the direction in which the experimentation should proceed.'" *In re Wands*, 858 F.2d at 737, 8 U.S.P.Q. 2d at 1404; M.P.E.P. § 2164.06. "[A]n extended period of experimentation may not be undue if the skilled

artisan is given sufficient direction or guidance." *In re Colianni*, 561 F.2d 220, 224, 195 U.S.P.Q. 150, 153 (C.C.P.A. 1977); M.P.E.P. § 2164.06. Furthermore, when analyzing the enabled scope of a claim, the teachings of the specification must not be ignored because claims are to be given their broadest reasonable interpretation that is consistent with the specification. In addition, the scope of enablement must only bear a "reasonable correlation" to the scope of the claims. M.P.E.P. § 2164.08 (citing *In re Fisher*, 427 F.2d 833 (C.C.P.A. 1970)).

Applicant respectfully traverses this rejection in light of the current amendments and the arguments advanced above including but not limited to those citing *Geneva Pharmaceuticals*, 68 U.S.P.Q.2d at 1873 and *In re Swinehart*, 169 U.S.P.Q. at 226. In addition, the Office Action suggests that "any and all 'enantiomer, isomer, tautomer, prodrug, free base or salt' of omeprazole" are insufficiently described or enabled. In light of the present amendments to claim 191, made without admitting or conceding in any manner that the rejected claims fail to comply with 35 U.S.C. § 112, second paragraph and solely to expedite the prosecution of the present application, Applicant submits that this rejection is now moot and that one of skill in the art, based upon the prior art and the disclosure as filed, would be able to practice the invention as presently claimed.

Therefore, in light of the claims as currently amended and the foregoing arguments, Applicant submits that the scope of the claims is enabled. Applicant respectfully requests that this rejection be withdrawn.

## III. THE REJECTION UNDER 35 U.S.C. 102(b) SHOULD BE WITHDRAWN.

The Office Action dated December 21, 2006, rejected claims 151-154, 156-159, 163, 165-170, 172 and 175 under 35 U.S.C. § 102(b) as being anticipated by WO 97-25066 ("Depui") or JP 05-255088 ("Oishi") supplemented with Horowitz. Applicant respectfully traverses this rejection.

M.P.E.P. § 2131 provides that "[a] claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described in a single prior art reference." *Verdegaal Bros. v. Union Oil Co. of California*, 814 F.2d 628, 631, 2 U.S.P.Q.2d 1051, 1053 (Fed. Cir. 1987). Furthermore, "[t]he identical invention must be shown in as complete detail as contained in the ... claim." *Richardson v. Suziki Motor Co.*, 868 F.2d 1226,

1236, 9 U.S.P.Q.2d 1913, 1920 (Fed. Cir. 1989). Lastly, "the elements must be arranged as required by the claim..." *In re Bond*, 910 F.2d 831, 15 U.S.P.Q.2d 1566 (Fed. Cir. 1990). Applicant respectfully submits that none of Depui, Oishi or Horowitz disclose each and every element of Applicant's claims as amended and therefore cannot anticipate said claims.

Applicant's pending claims contain the following limitations: omeprazole or a salt thereof in a total amount of about 1 mg to about 100 mg at least a portion of which is not enteric coated; at least one buffering agent comprising sodium bicarbonate; the composition being a finished dosage form; and the composition contains no aluminum glycinate or aluminum hydroxide sodium bicarbonate co-precipitate. Oishi discloses enteric coated preparations having a core containing a benzimidazole compound and small amounts of aluminum hydroxide-sodium bicarbonate co-precipitate surrounded by 1-2 layers of undercoating with an enteric coating thereupon. Oishi does not disclose a finished dosage form having omeprazole, at least a portion of which is not enteric coated. While Oishi does discloses an intermediate core that is not enteric coated, the disclosed core is not a finished dosage form. Oishi expressly states that such a core is coated with an enteric coating agent. (See e.g. page 2). In addition, Oishi does not teach compositions that contain no aluminum hydroxide-sodium bicarbonate co-precipitate or aluminum glycinate. Therefore, each and every element of Applicant's claims are not disclosed in Oishi. Applicant respectfully submits that the rejection is unsupported by the art and should be withdrawn.

Depui also fails to teach each limitation of Applicant's pending claims. First, Depui states that its enteric coated formulations do not disintegrate in the stomach. Therefore, one would not expect that Depui's formulations would meet the pharmacokinetic limitations of Applicant's claims. For example, Depui specifically states that its enteric coating makes "the pellets of the dosage form ***insoluble in acidic media***, but disintegrating/dissolving in near neutral to alkaline media such as, for instance the liquids present in the proximal part of the small intestine, where dissolution of the proton pump inhibitor is desired" (emphasis added). Depui at p. 20, ll. 25-28. Additionally, Depui teaches that the "enteric coating layer(s) covering the individual units of the acid susceptible proton pump inhibitor ("PPI") has properties such that the compression of the units into a tablet does not significantly affect the acid resistance of the individually enteric coating layered units." *Id.* at p. 5, ll. 19-22. Moreover, Depui states:

> If the enteric coating layer does not withstand the compression of the pellets into a tablet the susceptible active substance will be destroyed upon administration by penetrating acidic gastric juice, *i.e.*, the acid resistance of the enteric coating layer of the pellets will not be sufficient in the tablet after compression.

*Id.* at p. 4, ll. 8-11. Based on these admonitions, the skilled person at the time of the invention would not have expected absorption of the PPI from Depui's enteric coated compositions to occur within 30 minutes as claimed. As such, Depui fails to teach all the limitations of claims 1-25, expressly or inherently and, therefore, does not anticipate these claims.

Second, Applicant has amended claim 151 and 191 to include the limitation that at least a portion of the omeprazole is not enteric coated, which is also not taught by Depui. In fact, Depui specifically teaches away from compositions comprising proton pump inhibitor that is not enteric coated:

> Some gastric acid suppressing agents, such as proton pump inhibitors, are susceptible to degradation/transformation in acid reacting and neutral media. In respect of the stability properties, ***it is obvious*** that one of the active substances being a proton pump inhibitor ***must*** be protected from contact with acid gastric juice by an enteric coating layer.

Depui at p. 3, ll. 25-28 (emphasis added).

Third, the Examiner's reliance on Horowitz as allegedly illustrating Applicant's claimed blood level limitation not mentioned in Oishi or Depui, *i.e.* an "average plasma concentration of the omeprazole of at least 0.1 μg/ml .... within about 30 minutes after administration," is misplaced for at least the following reasons. As set forth in § 2131.01 III of the M.P.E.P., in order to make a showing of inherency, the "***evidence*** must make clear that the missing descriptive matter is ***necessarily present*** in the thing described in the reference, and that it would be so recognized by persons of ordinary skill" (emphasis added). Horowitz is directed to *liquid, non-enteric coated* compositions. Depui, on the other hand, is directed to *solid, enteric coated* compositions. As described above, Depui's dosage forms are enteric coated with a material that makes the PPI "insoluble in acidic media, but disintegrating/dissolving in near neutral to alkaline media such as, for instance the liquids present in the proximal part of the small intestine, where dissolution of the proton pump inhibitor is desired." Depui at p. 20, ll. 25-28. As such, the enteric coated PPI would not be available for absorption until after the enteric coated PPI passes

through the stomach and enters the small intestine. Consequently, it is speculative at best to compare Depui's solid forms to Horowitz's liquid dosage forms.

Moreover, Horowitz employs about 4,032 mg of sodium bicarbonate per 90 mg of omeprazole—an amount of buffer that could not practically be used in a solid dosage form. Depui, on the other hand only discloses a total buffering agent to total PPI weight ratio of up to about 2:1 (or 180 mg buffer per 90 mg omeprazole). To assume that 180 mg of sodium bicarbonate would provide the same protection of a PPI in gastric acid as 4,032 mg is speculative. Therefore, Horowitz cannot be used to demonstrate the pharmacokinetic characteristics of Depui's enteric coated compositions.

Further, it is well known that a given drug substance will have different absorption rates and times of onset depending on the dosage form and excipients, and that these differences are a function of both the formulation and the route of administration. *See e.g.* Ansel et al., Pharmaceutical Dosage Forms and Drug Delivery Systems, Williams & Wilkins, 1995, pp. 77 (attached as Exh. 3). ("An individual drug substance may be formulated into multiple dosage forms which result in different drug absorption rates and times of onset, peak, and duration of action."). This is because, for example, a solid dosage form must first disintegrate and then dissolve before the PPI is released, and only after this occurs can the PPI be absorbed (assuming that it has not been degraded by stomach acid). Accordingly, Horowitz's liquid disclosure provides no meaningful evidence relevant to the pharmacokinetic performance of Depui's solid dosage form, and the Examiner's anticipation rejection should be withdrawn.

For the foregoing reasons, Applicant submits that no *prima facie* case of anticipation has been established and respectfully requests withdrawal of this rejection.

## IV. THE REJECTION UNDER 35 U.S.C. 103(a) SHOULD BE WITHDRAWN.

The Office Action dated December 21, 2006 rejected claims 151-154, 156-159, 163, 165-170, 172-178, 180 and 182-236 under 35 U.S.C. § 103(a) over U.S. Patent No. 4,613,497 ("Chavkin") in view of U.S. Patent No. 4,508,905 ("Junggren") or Depui or Oishi supplemented with Horowitz further in view of Parachini, *Two New Drug Treatments Offer Hope to Ulcer Sufferers*, Los Angeles Times, Los Angeles, CA, August 30, 1988, page 1 ("Parachini") and Waring, *Questions and Answers about Medication and GERD*, DIGESTIVE HEALTHCARE OF GEORGIA; available at: http://www.aboutgerd.org/MedQA.html ("Waring"). Applicant

respectfully traverses the rejection and respectfully requests that the rejection be withdrawn in light of the arguments set forth below and the present amendments to the claims.

Please note that for the purposes of the response, Applicant assumes that the Office Action inverted the Chavkin and Junggren reference names in the first two sentences of page 6.

To establish a *prima facie* case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine the reference teachings. Second, there must be a reasonable expectation of success. Finally, the references when combined must teach or suggest all the claim limitations. *See* M.P.E.P. § 2143.

The burden of establishing a *prima facie* case of obviousness lies with the PTO. In determining obviousness, one must focus on the invention as a whole. *Symbol Technologies Inc. v. Opticon, Inc.*, 935 F.2d 1569, 1577-78, 19 U.S.P.Q. 2d 1241 (Fed. Cir. 1991). The primary inquiry is: "[w]hether the prior art would have suggested to one of ordinary skill in the art that this process should be carried out and would have had a reasonable likelihood of success ... Both the suggestion and the expectation of success must be found in the prior art, not the applicant's disclosure." *In re Dow Chemical*, 837 F.2d 469, 473, 5 U.S.P.Q. 2d 1531 (Fed. Cir. 1988).

As will be discussed in detail below, Applicant submits that no *prima facie* case of obviousness has been established because the references do not disclose each and every element of the claimed invention, and because no motivation to combine these references exists.

**A. <u>The references when combined do not teach or suggest all claim limitations.</u>**

Again, to establish a *prima facie* case of obviousness, all the claim limitations must be taught or suggested by the prior art. *See, e.g.*, M.P.E.P. § 2143.03 ("All words in a claim must be considered in judging the patentability of that claim against the prior art." *See In re Wilson*, 424 F.2d 1382,1385, 165 U.S.P.Q. 494 (C.C.P.A. 1970)). In this case, none of the references cited by the Office Action teach or suggest all of the claim limitations. Particularly, none of the references, alone or in combination, an orally deliverable pharmaceutical composition comprising about 1 mg to about 100 mg omeprazole, at least a portion of which is not enteric coated, and sodium bicarbonate, in a solid dosage form, comprising no aluminum glycinate and no aluminum hydroxide-sodium bicarbonate co-precipitate; wherein upon oral administration to

a group of subjects, they exhibit an average plasma concentration of the omeprazole of at least about 0.1 μg/ml at any time within about 30 minutes after administration.

**1.** Chavkin does not teach or suggest all claim limitations

Chavkin discloses a substantially anhydrous foamable composition capable of forming a substantially stable foam on contact with water, and has particular application in contraceptives and another application as "gastric-intestinal depots." Chavkin discloses a gastric antiacid film-coated tablet containing potassium bicarbonate, citric acid, sodium alginate, dicalcium phosphate and dihydrate.

Chavkin does not teach all the limitations of Applicant's pending claims. First, Chavkin does not disclose a solid form of a composition. Second, Chavkin does not disclose the use of omeprazole, at least a portion of which is not enteric coated. Third, Chavkin does not teach or suggest compositions comprising sodium bicarbonate. Fourth, Chavkin does not teach an "average plasma concentration of the omeprazole of at least 0.1 μg/ml .... within about 30 minutes after administration."

**2.** Junggren does not teach or suggest all claim limitations

Junggren discloses compounds of the formula of a substituted 2-(-benzimidazolyl)pyridine, which can be used in the treatment of peptic ulcer disease. Junggren provides that the object of the invention is to obtain compounds which affect gastric acid secretion.

Junggren does not teach all the limitations of Applicant's pending claims. First, Applicant's claims differ from Junggren by requiring both omeprazole and sodium bicarbonate in one solid formulation. Second, Junggren does not disclose a solid formulation of omeprazole, at least a portion of which is not enteric coated. Third, Junggren does not teach an "average plasma concentration of the omeprazole of at least 0.1 μg/ml .... within about 30 minutes after administration."

**3.** Parachini does not teach or suggest all claim limitations

According to the Office Action, Parachini teaches that an effective product would incorporate "'conventional [antacids] already on the market with a chewable or fizzy form of cimetidine.'"

Parachini does not teach or suggest all the limitations of Applicant's pending claims. First Parachini provides no dosage ranges for buffers and proton pump inhibitors. Second, Parachini does not disclose omeprazole and sodium bicarbonate in one solid oral formulation. Third, Parachini does not disclose a solid formulation of omeprazole, at least a portion of which is not enteric coated. Fourth, Parachini does not teach an "average plasma concentration of the omeprazole of at least 0.1 μg/ml .... within about 30 minutes after administration."

**4.** Waring is not available as a reference and does not teach or suggest all claim limitations

Waring is a printout of a website "last updated July 3, 2005." According to the Office Action, "Waring shows that it is a well-known procedure to take an antacid with a PPI." First, Applicant submits that this reference is not prior art, as the apparent date of the reference is after the filing date of this Application, March 10, 2004. Second, even if Waring were prior art, which it is not, it does not teach or suggest each limitation in Applicant's pending claims. For example, Waring does not disclose a solid dosage form comprising both a proton pump inhibitor and a buffer. Instead, Waring discloses using an antacid to supplement an independently administered proton pump inhibitor. In addition, Waring does not disclose a solid formulation of omeprazole at least a portion of which is not enteric coated. Waring also fails to teach or suggest an "average plasma concentration of the omeprazole of at least 0.1 μg/ml .... within about 30 minutes after administration."

**5.** Depui, Oishi and Horowitz do not teach or suggest all claim limitations

As discussed above, Depui is directed exclusively to enteric coated compositions and states that its formulations do not disintegrate in the stomach. Oishi discloses enteric coated preparations that are not in a finished solid dosage form, having a core containing a benzimidazole compound and small amounts of aluminum hydroxide-sodium bicarbonate co-precipitate surrounded by 1-2 layers of undercoating with an enteric coating thereupon. Horowitz only discloses administration of liquid compositions of omeprazole, not solid compositions. Horowitz also teaches that for clinical use the omeprazole would be formulated in enteric coated granules and not administered with bicarbonate. *See* Horowitz at p. 793. Horowitz also teaches an amount of sodium bicarbonate per 90 mg of omeprazole that could not be used practically in solid dosage form. Therefore, Horowitz cannot be used to demonstrate the pharamacokinetic characteristics of Depui's enteric coated compositions.

As set forth *supra*, Depui, Oishi and Horowitz do not teach all claim limitations as currently amended. First, in contrast to Depui and Oishi, Applicant's claims require at least a portion of the omeprazole in the final dosage form to not be enteric coated. Second, unlike Oishi, Applicant's claims are directed to compositions that do not contain aluminum hydroxide-sodium bicarbonate co-precipitate. Third, claims 151 and 191 and claims depending therefrom require an "average plasma concentration of the omeprazole of at least 0.1 μg/ml .... within about 30 minutes after administration." Depui and Oishi do not expressly or inherently disclose this limitation. Fourth, unlike Horowitz, Applicant's claims teach the administration of omeprazole and sodium bicarbonate in the same *solid* dosage form.

Moreover, Depui, Oishi and Horowitz actually teach away from the claimed invention: Depui and Horowitz inform one to enteric coat the dosage form, and Horowitz discloses that for clinical use the omeprazole would be formulated in enteric coated granules and not administered with bicarbonate. *See* Horowitz at p. 793. Thus, when the teachings of Depui and Horowitz are taken as a whole, as is required when examining potential prior art references, each of them teach away from the use of a solid dosage form comprising non-enteric coated PPI and buffer as claimed by Applicant. Therefore, Depui, Oishi and Horowitz do not teach or suggest Applicant's claimed inventions.

**6.** Chavkin in view of Junggren or Depui or Oishi supplemented with Horowitz further in view of Parachini and Waring do not teach or suggest all claim limitations

Chavkin in view of Junggren, Depui or Oishi supplemented with Horowitz further in view of Parachini and Waring do not disclose the claimed invention as none of these references either alone or in combination teach treating or preventing an acid-caused gastrointestinal disorder by orally providing a solid pharmaceutical composition form comprising a proton pump inhibitor, a portion of which is not enteric coated and sodium bicarbonate.

Since the references suggested by the Office Action do not disclose all limitations of the Applicant's claims, a *prima facie* case of obviousness has not been shown. Accordingly, the claimed invention is not obvious over Chavkin in view of Junggren or Depui or Oishi supplemented with Horowitz further in view of Parachini and Waring, as each and every element of amended claims 151-154, 156-159, 163, 165-170, 172-178, 180 and 182-236 are not disclosed in any combination of these references.

**B. The office action fails to identify any suggestion or motivation to combine the references.**

Furthermore, even if each and every limitation were disclosed in Chavkin in view of Junggren or Depui or Oishi supplemented with Horowitz further in view of Parachini and Waring, which is denied, Applicant respectfully submits that no motivation to combine the references exists. As previously set forth, to establish a *prima facie* case of obviousness when combining multiple references, there must be an explicit teaching, suggestion or motivation to combine the references. *Winner Int'l Royalty Corp v. Wang*, 202 F. 3d. 1340, 1348-49, 53 U.S.P.Q. 2d 1580 (Fed. Cir. 2000). Obviousness is tested by "what the combined teachings of the references would have suggested to those of ordinary skill in the art." *In re Keller*, 642 F.2d 413 (C.C.P.A. 1981). It "cannot be established by combining the teachings of the prior art to produce the claimed invention, absent some teaching or suggestion supporting the combination." *ACS Hosp. Sys., Inc. v. Montefiore Hospital*, 732 F.2d 1572 (Fed. Cir. 1984). The "teachings of references can be combined *only* if there is some suggestion or incentive to do so." *Id.* One cannot use hindsight reconstruction to pick and choose among isolated disclosures in the prior art to depreciate the claimed invention. *In re Fine*, 837 F.2d 1071 (Fed. Cir. 1988).

Moreover, the Federal Circuit has explicitly stated that this teaching must be "clear and particular." *Id.* The absence of such teachings to combine references is dispositive of an obviousness inquiry. *Id.* Indeed, the M.P.E.P. specifically states that "[t]he mere fact that references can be combined or modified does not render the resultant combination obvious unless the prior art also suggests the desirability of the combination." M.P.E.P. § 2143.01 (emphasis in original).

Applying this settled rule, the Office Action dated December 21, 2006 has failed to identify any teaching, suggestion or motivation within Chavkin in view of Junggren or Depui or Oishi supplemented with Horowitz further in view of Parachini and Waring, that would compel a person of ordinary skill in the art to combine the references and obtain the claimed invention. The identification of the specific teaching or motivation to combine references is a necessary component to establish a *prima facie* case of obviousness. In the absence of "clear and particular" teachings to combine references, a *prima facie* showing of obviousness has not been made and the rejection should be withdrawn. *In re Chu*, 66 F.3d 292, 299, 36 U.S.P.Q. 2d 1089 (Fed. Cir. 1995).

The claims currently pending in examination specify the oral administration of a solid dosage form of omeprazole, at least a portion of which is not enteric coated, and sodium bicarbonate, comprising no aluminum glycinate and no aluminum hydroxide-sodium bicarbonate co-precipitate, wherein upon oral administration to a group of subjects, they exhibit an average plasma concentration of the omeprazole of at least about 0.1 μg/ml at any time within about 30 minutes after administration. As stated above, Waring is not prior art. Thus, Waring cannot be used to provide a motivation to combine references. Moreover, Waring does not provide a motivation to combine the references to arrive at the claimed invention. In addition, none of the other references relied on by the Examiner provide any motivation to combine their teachings in such a manner as to arrive at the invention currently claimed. In fact, as discussed above, the references as a whole teach away from the claimed invention. Because there is a complete absence of any teaching, suggestion or motivation to combine the references as suggested by the Office Action, a *prima facie* case of obviousness has not been shown. Accordingly, the claimed invention is not obvious over the cited references.

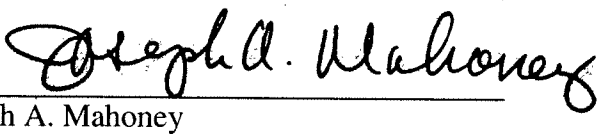
Therefore, Applicant submits that no *prima facie* case of obviousness exists, and amended claims 151 and 191 are patentable over Chavkin in view of Junggren or Depui or Oishi supplemented with Horowitz further in view of Parachini and Waring. Furthermore, claims 152-154, 156-159, 163, 165-170, 172-178, 180, 182-190 and 192-236 are patentable over the references cited in the Office Action as they depend on amended claim 151 and 191. Consequently, Applicant respectfully requests withdrawal of this rejection.

**Conclusion**

For at least the foregoing reasons, it is respectfully submitted that claims 151-154, 156-159, 163, 165-170, 172-178, 180 and 182-236 are in condition for allowance. Early and favorable consideration is respectfully requested, and the Examiner is encouraged to contact the undersigned with any questions or to otherwise expedite prosecution. Further, none of Applicant's amendments or cancellations are to be construed as dedicating any such subject matter to the public, and Applicant reserves all rights to pursue any such subject matter in this or a related patent application.

Kindly contact the undersigned with any questions or to otherwise expedite prosecution.

Respectfully submitted,



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